

Endou et al.
U.S.S.N. 09/424,347
Amendment Dated March 24, 2003
Reply to Office Action of October 22, 2002
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Amendments To The Specification:

Kindly amend the header on page 3, line 13, as follows:

BEST MODE FOR CARRYING OUT THE INVENTION

Kindly amend the paragraph starting at page 3, line 21, as follows:

C¹ (A) The protein whose amino acid sequence is shown in SEQUENCE No. SEQ ID NO: 1.

Kindly amend the paragraph starting at page 3, line 22, as follows:

C² (B) The proteins whose amino acid sequences are identical to that shown in SEQ ID NO: SEQUENCE No. 1 except that several amino acid residues are deleted, substituted or added in it.
Despite of these changes, the protein must possess the ability to transport organic anions.

Kindly amend the paragraph starting at page 4, line 3, as follows:

C³ (C) The protein whose amino acid sequence is shown in SEQ ID NO: SEQUENCE No. 2.

Kindly amend the paragraph starting at page 4, line 4, as follows

C⁴ (D) The proteins whose amino acid sequences are identical to that shown in SEQ ID NO: SEQUENCE No. 2 except that several amino acid residues are deleted, substituted or added in it.
Despite of these changes, the protein must possess the ability to transport organic anions.

Kindly amend the paragraph starting at page 4, line 10, as follows

C⁵ (a) The DNA whose nucleotide sequence is shown in SEQ ID NO: SEQUENCE No. 1.

Kindly amend the paragraph starting at page 4, line 11, as follows

C⁶ (b) DNAs which can hybridize the DNA shown in SEQ ID NO: SEQUENCE No. 1 in stringent condition, and encode the proteins possessing the ability to transport organic anions.

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Kindly amend the paragraph starting at page 4, line 13, as follows

C7 (c) The DNA whose nucleotide sequence is shown in SEQ ID NO: SEQUENCE No. 2.

Kindly amend the paragraph starting at page 4, line 14, as follows

C8 (d) DNAs which can hybridize the DNA shown in SEQ ID NO: SEQUENCE No. 2 in stringent condition, and encode the proteins possessing the ability to transport organic anions.

Kindly amend the paragraph starting at page 5, line 7, as follows:

C9 The SEQ ID NO: SEQUENCE NO. 1 shown in the table depicts the total nucleotide sequence of rat OAT1 cDNA (approximately 2.2 kb) with the deduced amino acid sequence (551 amino acid residue) encoded by the open reading frame of rat OAT1 cDNA.

Kindly amend the paragraph starting at page 5, line 10, as follows:

C10 The SEQ ID NO: SEQUENCE NO. 2 shown in the table depicts the total nucleotide sequence of human OAT1 cDNA (approximately 2.2 kb) with the deduced amino acid sequence (563 amino acid residue) encoded by the open reading frame of human cDNA.

Kindly amend the paragraph starting at page 5, line 20, as follows:

C11 In addition to the amino acid sequence shown in SEQ ID NO: SEQUENCE NO. 1 and SEQ ID NO: NO. 2, the present invention includes the following proteins. Proteins whose amino acid sequences are identical to that shown in SEQ ID NO: SEQUENCE No. 1 except that several amino acid sequence of these proteins are acceptable when the product proteins possess the ability to transport organic anions. Usually, numbers of the changed amino acid residues are between one to 110, preferably 1 to 55. These amino acid sequences show 80%, preferably 90%, identity to that shown in SEQ ID NO: SEQUENCE NO. 1 or SEQ ID NO: NO. 2.

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Kindly amend the paragraph starting at page 6, line 3, as follows:

In addition to the DNAs with the nucleotide sequences shown in SEQ ID NO:

SEQUENCE NO. 1 and SEQ ID NO: NO. 2, the present invention includes DNAs which can hybridize the cDNA shown in SEQ ID NO: SEQUENCE NO. 1 and SEQ ID NO: NO. 2. The proteins encode by these DNAs must possess the ability to transport organic anions. Usually, these DNAs show more than 70%, preferably 80%, identity to those shown in SEQ ID NO:

SEQUENCE NO. 1 or SEQ ID NO: NO. 2. These DNAs include mutated genes found in nature, artificially ? mutated genes and the genes derived from other species of living cells.

Kindly amend the paragraph starting at page 8, line 3, as follows:

Based on the sequence of this invention shown in SEQ ID NO: SEQUENCE NO. 1 and

SEQ ID NO: NO. 2, sets of PCR (polymerase chain reaction) primers can be designed by which cDNA probes can be synthesized to search the cDNA or genomic library.

Kindly amend the paragraph starting at page 9, line 1, as follows:

The cDNAs which can be used for the above mentioned purpose are not restricted to those shown in SEQ ID NO: SEQUENCE NO. 1 and SEQ ID NO: NO. 2. Since each amino

acid is encoded by several types of codon, cDNAs which encode the proteins with the amino acid sequences shown in SEQ ID NO: SEQUENCE NO. 1 and SEQ ID NO: NO. 2 can be designed based on information of codons. Any codon, which encode the desired amino acid, can be selected, and cDNAs inducing more efficient expression may be designed considering the codon preference in the host cells. The designed cDNAs can be obtained by chemical DNA synthesis, digestion and ligation technique, and site-directed mutagenesis method. The methods of the site directed mutagenesis are described elsewhere (Mark, D.F., et al., Pro Nat Aca Sci, vol 81, 5662-5666, 1984)

Kindly amend the paragraph starting at page 12, line 22, as follows:

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C¹⁵

The nucleotide SEQ ID NO: SEQUENCE NO. 1 is the sequence of OAT1.

C¹⁶

Kindly amend the paragraph starting at page 17, line 13, as follows:

The sequence of human OAT1 in both nucleotide and amino acid level is shown in SEQ ID NO: SEQUENCE NO. 2.

Kindly amend the Abstract, as follows:

C¹⁷

A protein capable of transporting organic anions having amino acid sequences represented by SEQ SEQ ID NO: 1 or 2 or amino acid sequences derived therefrom by deletion, substitution or addition of one or more amino acid residues; and a gene coding for the protein. The protein and gene therefortherefore are useful *in vitro* analysis of drug release and drug-drug interactions and development of method for screening drugs useful for preventing nephrotoxicity.